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10/817,423	04/02/2004	Thomas R. Scott	CXU-407	1563

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/817,423	SCOTT ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-21 and 43-56* is/are pending in the application.

4a) Of the above claim(s) *17,50,53 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16 and 18-21,43-49,51,52,54 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/14/05, is acknowledged.

2. Claims 15-21 and 43-56 are pending.

3. A clear and obvious typographical error occurred in the Non-Final Office Action wherein claim 17 which reads on non-protein second component (non-elected species) was included in the examined claims. Claim 17 will not be examined along with elected group I as is with claims 50, 53 and 56.

4. Claims 17, 50, 53 and 56 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

5. Claims15-16, 18-21, 43-49, 51-52 and 54-55 are under consideration in the instant application as they read on a therapeutic composition comprising a polypeptide capable of binding to at least one of α6β1 integrin receptor and α6β4 integrin receptor and a second component.

6. Applicant's IDS, filed 11/14/05, is acknowledged, however, references 4, 7-10, 14 and 16 have been crossed out because they are duplicates of the same references cited on the PTO-892 Form mailed 8/12/05.

7. The following new ground of rejection is necessitated by the amendment submitted 11/14/05.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 48-49, 51-52 and 54-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The recitations that "wherein the at least one of α6β1 integrin receptor and α6β4 integrin receptor specifically binds to a second polypeptide comprising a segment consisting of SEQ ID NO:2/4/6" in claims 48, 51 and 54 respectively, are ambiguous and indefinite. It is unclear how the bound α6β1 integrin receptor and α6β4 integrin receptor to a first polypeptide would also specifically bind to a second polypeptide. Specially, because the 1st and 2nd polypeptide are derive from the same laminin-5 α3 chain. Therefore, the binding site of the integrin receptors would be bound with the 1st polypeptide of laminin-5 α3 chain and not available to bind to the 2nd polypeptide of laminin-5 α3 chain.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 48-49, 51-52 and 54-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrases "wherein the at least one of α6β1 integrin receptor and α6β4 integrin receptor specifically binds to a second polypeptide comprising a segment consisting of SEQ ID NO:2/4/6" claimed in claims 48, 51 and 54, respectively represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 11/14/05 does not point to the specification for support for the newly added limitations "wherein the at least one of α6β1 integrin receptor and α6β4 integrin receptor specifically binds to a second polypeptide comprising a segment consisting of SEQ ID NO:2/4/6" as claimed in claims 48, 51 and 54. However, the specification does not provide a clear support for such limitations. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

12. In view of the amendment filed on 11/14/05, only the following rejections are remained.

13. Claims 15-16, 18-21, 43-49, 51-52, and 54-55 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide **enablement** for a fused or chimeric polypeptide "comprising" a fused or chimeric polypeptide comprising a first component "including" a polypeptide that specifically binds to a least one of α6β1 integrin receptor and α6β4 integrin receptor, wherein the polypeptide "comprises" the "G3 subdomain of the laminin-5 α3 chain" or a "fragment, homolog or ortholog thereof" and a second component chemically bound to said first component wherein said second component includes an "agent" for use in the destruction of or neutralization of a pathogen comprising an least one of α6β1 integrin receptor and α6β4 integrin receptors on the surface of the pathogen in claim 15 , wherein the second component is any polypeptide in claim 16, wherein the first component comprises at "least about 70% sequence identity" with SEQ ID NO: 2, 4 or 6, in claims 19-21 or at "least about 90% sequence identity" with SEQ ID NO: 2, 4 or 6, in claims 43-45 or wherein the first component "comprises" a segment consisting of SEQ ID NO: 6 in claim 47; a fused or chimeric polypeptide comprising a first component "comprising" a first polypeptide, wherein the first polypeptide "comprises" at "least a segment of the G-domain of a laminin-5 α3 chain" and the first polypeptide specifically binds to at least one of α6β1 integrin receptor and α6β4 integrin receptor, wherein the at least one of α6β1 integrin receptor and α6β4 integrin receptor specifically binds to a second polypeptide comprising a segment consisting of SEQ ID NO:2, 4, or 6 and any "second component" chemically bond to said first component wherein said second component includes an agent for use in the destruction or neutralization of a pathogen

comprising at least one of α6β1 integrin receptor and α6β4 integrin receptor on the surface of the pathogen in claims 48, 51, and 54, wherein the second component is a polypeptide in claims 49, 52, and 55. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 8/12/05.

Since Applicant's arguments fail to address all the issues presented in the previous Office Action, the issues are reiterated here again.

At issue is whether or not the claimed composition would function as therapeutic composition. Although Applicant's specification describes certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical functional use is currently available form for humans or animals. The US 20020058336 publication teaches that the alpha6/beta1 integrin is expressed on platelets, lymphocytes, monocytes, thymocytes and epithelial cells, on which it functions as a laminin receptor for laminin-1, laminin-2 and laminin-4 *in vivo*. It is also a receptor for laminin-5, but not *in vivo* (see page 3, paragraph 19). Cochlovius *et al* (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells *in vivo* seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously *in vitro* but a fairly high portion of them still fail *in vivo*. Thus, it is not clear that reliance on the *in vitro* studies accurately reflects the relative mammal and human efficacy of the claimed therapeutic strategy. The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective *in vivo* mammalian including human therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the fused or chimeric G3 subdomain by administering to a mammal a therapeutically effective amount of therapeutic composition. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of any therapeutic composition comprising the fused or chimeric G3 subdomain of the laminin-5 α3 are fraught with uncertainties. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to use in humans or animals. Ex parte Maas, 9 USPQ2d 1746. There must be a rigorous correlation of pharmacological activity between the disclosed *in vitro* use and an *in vivo* use to establish practical therapeutic use.

Further, at issue whether the G3 subdomain linked to a therapeutic moiety such as IL-2 would destroy or neutralize a pathogen. It appears that applicant is using the claimed polypeptide comprising G3 for target delivery of a drug. The specification fails to provide example wherein the IL-2 can destroy or neutralize any pathogen. The skilled artisan would not expect IL-2, a hormone-like substance released by stimulated T lymphocytes, causes activation and differentiation of other T lymphocytes independently of antigen to function in destroying or neutralizing any pathogen. However, in view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the polypeptide as claimed, and absence of

working examples providing evidence which is reasonably predictive that the claimed composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed antibodies with a reasonable expectation of success. Kahan states that, at the time of the invention, "no in vitro immune assay predicts or correlates with in vivo immunosuppressive efficacy; hence, there is no surrogate immune parameter as a basis of immunosuppressive efficacy and/or for dose extrapolation from in vitro systems to in vivo conditions" (Curr. Opin. Immuno. 4:553:560, 1992; see entire document, particularly page 558, column 2) making the in vivo efficacy of an immunosuppressive compound tested solely in vitro unpredictable.

Also, claim 15, recites any "pathogen", it is unclear which patients would be candidates for *in vivo* treatment with a chimeric polypeptide comprising IL-2 and when a patient would be given such treatments/chimeric comprising IL-2. Further, claim 15 recites pathogens comprising at least one of $\alpha 6\beta 1$ integrin receptors and $\alpha 6\beta 4$ integrin receptors on the surface of the pathogen. However, the specification has failed to identify any pathogen (microorganisms) that expresses either $\alpha 6\beta 4$, $\alpha 6\beta 1$ or both integrin receptors. It is noted that $\alpha 6\beta 4$-integrin is predominantly expressed in epithelium and it is a major component of hemidesmosomes that link the cytoskeleton to basement membrane through interaction with laminin-5.

Further, Applicant has not provided sufficient biochemical information that distinctly identifies such "G3 subdomain", "fragment, homolog or ortholog" and "at least about 70% sequence identity" other than SEQ ID Nos:2, 4 and 6. While any polypeptide capable of binding to at least one of $\alpha 6\beta 1$ integrin receptor and $\alpha 6\beta 4$ may have some notion of the activity of the "inhibitory agent", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such "agents", commensurate in scope with the claimed invention. The specification fails to provide any guidance on how to use any chimeric or fusion polypeptide comprising G3 subdomain that can be used to inhibit adhesion and proliferation of a target cell to a substrate. While the specification on pages 30-30 under examples 4 and 5 discloses that the G3 domain of rat laminin-5 $\alpha 3$ chain coated on wells inhibited proliferation of the cancer cells, however, no fusion polypeptide were used to target any pathogen (microorganism).

The terms "comprising" and "including" in base claim 15 is open-ended. It would leave the claims open for the inclusion of unspecified amino acids at either or both or the N-or C-termini of given sequence even in large amounts. See MPEP 2111.03. Besides the polypeptide comprising G3 subdomain of SEQ ID NO: 6, 4 and 2, there is insufficient guidance as to which amino acid segments within the polypeptide can be unique and retain a distinct functional capability of G3/$\alpha 6$ bearing integrin receptor. Since the amino acid sequence of a polypeptide determined its structural property, predictability of which amino acid fragment can retain the functional capabilities of the G3/$\alpha 6$ requires knowledge of, and guidance with regard to, which fragments in the polypeptide's sequence contribute to its function.

After a review of the specification with respect to the nature of "fragments" "analogs", "mutants", "homolog", and "alleles", the specification was not found to provide sufficient guidance to the skilled artisan as to how to make and use G3 "analogs", "mutant" , "ortholog", or "allele" commensurate in scope with the instant claims. In particular, it is noted that the specification on page 7 at paragraph 31 discloses that "analog" encompasses "a non-natural molecule substantially similar to either the entire reference protein or polypeptide or a fragment or allelic variant". Further, the specification on page 7, paragraph 32 indicates that "allele" encompasses a naturally-occurring sequence variation relative to the polypeptide sequence of the reference polypeptide. Also, the specification on page 6, paragraph 30, discloses that "homolog" includes polypeptides sequences including one or more substitutions, deletions, or insertions, located at positions of the sequence that do not alter the conformation or folding of the polypeptide. The term "mutant" is defined in the specification on page 6, under paragraph 29 to encompass base changes, deletions, insertions, inversions, translocations, or duplications. "Ortholog" is defined on page 5 of the specification to encompass polypeptide sequence with similar function to polypeptide sequence in an evolutionarily related species. Finally, the term "fragment" is defined on page 5, paragraph 27 of the specification to include an amino acid sequence of that protein that is shorter than the entire protein, but comprising at least about 25 consecutive amino acids of the full polypeptide.

Given the breadth encompassed by the instant claims, Applicant has not provided the skilled artisan with sufficient guidance as to the identity of all residues to be changed, to be left unchanged, to be deleted, or to have additional (unidentified) sequences inserted between. Without clear direction and guidance as to the nature of the changes made to a reference G3 sequence, the skilled artisan would be faced with undue experimentation to produce the immense number of "fragments" "homolog", and "ortholog" encompassed by the instant claims and determine if there were any operative embodiment that would result in the recited functional activity. Thus the specification does not appear to provide the skilled artisan with sufficient guidance to make and use such "fragments" and "homolog", commensurate in scope with the claimed invention of therapeutic composition encompassed by the claims. The specification offers no guidance as to what particular fragment, other than SEQ ID NOs:2, 4, and 6, are required to ensure the inhibition response. A myriad of polypeptide is encompassed by the claims.

It was well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities. For example, Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. The references demonstrate that event a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

Also, it is recognized in the art that ligands must posses significant structural and chemical complementarity to their target receptors (Kuntz, Science, 1992, Vol. 257:1078-1082, especially

page 10709, 2nd col., lines 1-4 and 9-12 under heading "Structure-Based Design) and that ligands generally bind to native states of proteins with little or no interaction with unfolded states (Miller et al, Protein Science, 1997, 6:2166-2179, especially page 2166, 2nd col., lines 18-20) and further that alterations in protein structure lead to alterations in bindings affinity proportional to the magnitude of the alteration (Miller et al, abstract, lines 2-4). Finally, Kuntz teaches that as little as 2% of compounds predicted to inhibit specific enzymztic or receptor systems actually shown inhibition in the micromolar range (page 1080, 3rd col.). The claims encompass alterations in protein folding because claims do permit deviation from the amino acid sequences of the G3 subdomain of SEQ ID NO: 6 for a non-native protein. It would be reasonable to conclude that alterations in polypeptide folding would lead to a large alteration in binding affinity.

The art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Applicant's arguments, filed 11/14/05, have been fully considered, but have not been found convincing.

Applicant submits that pending claims are directed to fused or chimeric proteins that are adequately described in the specification in conjunction with the information that was well known to persons of ordinary skill in the art as both how to make and how to use the claimed invention. Applicant submits that the polypeptide sequences specific to rat laminin described in the application as SEQ ID NO: 2, 4, and 6, as well as other known, homologous proteins that can be utilized to obtain polypeptides comprising the G3 subdomain of the laminin-5 α3 chain, e.g., mouse laminin-5, mus musculus laminin-5, artificial laminin-5 and human laminin-5 (¶41). Further such materials as well as sources for these materials are well known to one of skill in the art. Applicant refers to Kariya et al (IDS ref) who have described methods for forming smaller or truncated forms (i.e., fragments) of the G3 subdomain of the α3 chain. Further, Applicant submits that many homologous or orthologous α3 genes are well known in the art, all of which include the G3 subdomain. Applicant refers to NCBI GenBank database as an indication that a3 genes for mouse, human, bovine and dog are well known. Applicant further submits that it is well within the knowledge of one of ordinary skill in the art to translate these genetic sequences

via the well-known and publicly available orf's to polypeptide sequences comprising the G3 subdomain of the laminin-5 α3 chain. Applicant asserts that while aspects of making of the claimed invention, for example, blasting the desired specific sequence against other known sequence, transcribing the nucleotide sequence into the polypeptides, comparing sequence identities to the disclosed polypeptides, and the like, may require some experimentation, the level of experimentation required to make the claimed invention is not undue given the level of skill in the art and the teachings of the disclosure.

However, the instant fact pattern fails to indicate that a representative number of structurally related G-domain of a laminin-5 α3 chain molecule is disclosed in the specification. The artisan would not know the identity of a reasonable number of representative G-domain of a laminin-5 α3 chain falling within the scope of the instant claim and consequently would not have known how to make them. Further, any assay for finding a product is not equivalent to a positive recitation of how to make such a product. The specification does not provide any guidance or any working examples, thus the artisan would have been unable to make the claimed compound without undue experimentation. In order to satisfy 112, first paragraph, the specification has to teach how to make and use the polypeptides of the invention not how to identify the invention. Until the time when the at least about 70% or 90% sequence identity polypeptides or the fragments, homolog or ortholog of the G3 subdomain of the laminin-5 α3 chain are found, then one skill in the art can make them.

The Examiner notes that Kariya et al support the examiner's position that the amino acid residues change in the G3 domain in laminin-5 produce different biological effects on cells. Kariya et al attributed Lys-Arg-Asp sequence of COOH terminal 28 amino acids of the G3 domain of the α3 chain to loss of cell motility activity, while deletion of 83 amino acids lead loss of the cell motility activity. Importantly Kariya et al concludes that the G3 domain contains two distinct regions that differently regulate cell adhesion and migration. Since the amino acid sequence of a polypeptide determined its structural property, predictability of which amino acid fragment or variants can retain the functional capabilities of the G3/α6 requires knowledge of, and guidance with regard to, which fragments or variants in the polypeptide's sequence contribute to its function.

Applicant further asserts that the second component of the fused polypeptide are generally known to one of ordinary sill in the art as well as described in ¶ 59 and 61 of the specification. Applicant contends that there are many well known methods for chemically binding the two components to one another, for example, IL-2 has been described as a fusion partner with a different protein delivery system in Zhang et al. Further, other well known methods for forming fusion polypeptides such as those described herein include methods such as those described by Beck et al and Langnheim and Chen 2005.

The examiner agrees that it is within the knowledge of those skilled artisan to make a fusion polypeptide. However, since the first component is not enabled then the fusion polypeptide is not enabled too.

Regarding how to use, Applicant submits that the specification clearly details exemplary methods for how to bind disclosed materials to a pathogen including at least one of α6β1 integrin receptor and α6β4 integrin receptor. Further, Applicant submits that the specification clearly describes the second component of the polypeptides as an agent for use in the destruction or neutralization of a pathogen, and one of ordinary skill in the art would know how to use the disclosed pathogen, and one of ordinary skill in the art would know how to use the disclosed materials to destroy or neutralize the described pathogens. In particular, Applicant submits that IL-2 is a know agent capable of stimulating T cells, and specifically cytotoxic T-cells, when the T cells sees it antigen (i.e., the pathogen). One possible use for the chimeric and fusion proteins can be to deliver the second component directly to the pathogen. Applicant concludes that one of ordinary skill in the art would know that the disclosed polypeptides that include IL-2 as the second component could be used to deliver the IL-2 directly to the pathogen and thus enhance stimulating of the cytotoxic T –cells in the presence of the pathogen such as cancer cells, which can in turn lead to the destruction or neutralization of the pathogen. Further, this use can be carried out either in vivo or in vitro. Applicant provides an example wherein the materials could be utilized in determining pathogen proliferation in the presence of various concentrations of the fusion polypeptides, as described in the example section of the specification.

Contrary to applicant's assertions, the specification fails to make and use any fusion polypeptides encompassed in the claimed invention. Further and contrary to applicant's assertions the specification only used a recombinant rat laminin-5 α3 chain G3 domain protein of SEQ ID NO: 6 to illustrate MDA-MB-435 breast cancer cells inhibition. No in vivo or in vitro pathogen has been targeted with the claimed fusion or chimeric polypeptide. No T-cell has been shown to be stimulated with the claimed fusion polypeptide. No pathogen has be show to be destroyed or neutralized by the claimed polypeptide. The intended use of claimed G3 subdomain of LN-5 α3 chain fusion polypeptide that binds α6β1 and α6β4 on pathogen membranes, which stimulates T cells, to realize a therapeutic effect on the destruction and neutralization of pathogens is only a theory. There is no evidence of record that demonstrates that the claimed fusion polypeptide would destroy or neutralize any pathogen including MDA-MB-435 breast cancer cells. The fusion polypeptide of the invention is not anti-tumor agent. The specification fails to demonstrate that the fusion polypeptide of the invention directly relates to any pathogen expressing α6β1 and α6β4.

Applicant argues that among the many possible ways to use the inventions of the presently pending claims are both in vivo uses and in vitro uses. For example, in addition to the described in vivo therapeutic uses, the specification clearly describes how to use the materials ex vivo. Applicant refers to methods such as those described in the example section can be beneficial in developing treatment methods and materials through examination of the specific contribution the second component to the neutralization or destruction of a particular pathogen through examination of the proliferation of a pathogen in the presence of the materials as described in Examples 4 and 5 of the specification. Applicant concludes that the materials can be utilized in an in vitro method such as that specifically described in the example section to increase the understanding of communication and interactions between the various components of the fused or chimeric polypeptides.

Contrary to applicant's assertions the specification has not enabled the skilled artisan to make and used the claimed fusion or chimeric polypeptides as claimed. While the specification describes certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical intended use in currently available form for humans or animals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to use in humans or animals" (emphasis added). Ex parte Maas, 9 USPQ2d 1746.

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 9, 2006

Maher Haddad

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